AMENDMENTS

In the claims:

Please cancel claims 5 and 7 as being drawn to non-elected inventions. Also please cancel Claim 4. Please amend claims 1 and 2 as follows and please add new claims 8 and 9.

1.(currently amended) An isolated nucleic acid molecule comprising ~~at least 24 contiguous bases of~~ the nucleotide sequence ~~first disclosed in the NHP sequence~~ described in SEQ ID NO: 3.

2.(currently amended) An isolated nucleic acid molecule comprising a nucleotide sequence that:

(a) encodes the amino acid sequence shown in SEQ ID NO: 4; and

(b) hybridizes under highly stringent conditions to the nucleotide sequence of SEQ ID NO:3 or the complement thereof.

3.(original) An isolated nucleic acid molecule according to Claim 2 wherein said nucleotide sequence is present in cDNA.

4. - 5. (cancelled)

6.(original)An isolated nucleic acid molecule comprising a sequence encoding the amino acid sequence presented in SEQ ID NO:4.

7.(cancelled)

8. (new) An expression vector comprising a nucleotide sequence that encodes the amino acid sequence shown in SEQ ID NO:4.

9. (new) A cell comprising the expression vector of Claim 8.

RESPONSE

I. Status of the Claims

Claims 5 and 7 have been cancelled, as being drawn to non-elected inventions. Claim 4 has also been cancelled. Claims 1 and 2 have been amended and claims 8 and 9 have been added to better claim the present invention. As a result claims 1-3, 6, 8 and 9 are presently pending in this case.

II. Support for the Amended Specification and Claims

Claim 1 has been amended to better claim the present invention. Amended Claim 1 finds support in the application as originally filed with particular support being found in original Claim 1 and the sequence listing.

Claim 2 has been amended, as suggested by the Examiner, to better claim the present invention. Amended Claim 2 finds support in the specification as originally filed with particular support being found in original Claim 2 and at or about page 5 line 1-8.

Claim 8 has been added to better claim the present invention. New Claim 8 is supported by the specification as originally filed with particular support being found on or about page 14, lines 26-32.

Claim 9 has been added to better claim the present invention. New Claim 9 is supported by the specification as originally filed with particular support being found on or about page 14, line 32 through page 15, line 10.

As the amendments to claims 1 and 2 and new claims 8 and 9 are fully supported by the specification, the sequence listing and claims as originally filed, they do not constitute new matter. Entry therefore is respectfully requested.

III. Objection

The Action objects to original Claim 4 as it contains non-elected subject matter. As original Claim 4 has been cancelled, this objection has been overcome and should be withdrawn.

The Action also objects to the abstract of the application as being non-descriptive. Applicants point out that numerous issued U.S. Patents have an abstract **identical** to the present abstract.

Specifically, Applicants direct the Examiner's attention to issued U.S. Patent Nos. 6,433,153, 6,441,153, 6,441,154, 6,444,456 and 6,448,388. As issued U.S. Patents are presumed to meet all necessary PTO requirements, Applicants submit that the present abstract must also meet all necessary PTO requirements.

Applicants request that, since the objection has been overcome, this objection be withdrawn.

IV. Rejection of Claims Under 35 U.S.C. § 101

The Action first rejects the claims under 35 U.S.C. § 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. Applicants respectfully traverse.

Based on statements made in the Action the Examiner does not appear to recognize that Applicants have asserted that the sequences of the present invention encode a novel human metalloprotease (specifically ADAMTS 15). The Action (at page 4, line 10) suggests that the use of the term novel human protein and the abbreviation NHP is indicative of applicant's ignorance. However, in fact the use of the term novel human protein (NHP) does not originate due to ignorance, but rather these terms are used as a matter of convenience and to increase the efficiency and reduce the costs of patent preparation. The use of the identifier NHP, in no way obviates applicants assertions that the sequences of the present invention are metalloproteinases. Applicants respectfully submit that the similarity of the novel human metalloprotease encoded by the sequences of the present invention and metalloproteinases, especially zinc metalloproteases of the ADAMTS family was described in the specification at, among other locations, page 20, lines 1-2 and on page 2, line 4.

This belief is perhaps in part based on the Examiner's belief that there "is non-specific asserted utility because the specification does not describe any protease activity" (Action at page 3 last paragraph, lines 6-7). However, Applicants respectfully submit that this emphasis is misplaced as it has long been established that "there is no statutory requirement for the disclosure of a specific example". *In re Gay*, 135 USPQ 311 (C.C.P.A. 1962). Applicants assertion of the stated utility is legally sufficient and should control the utility analysis unless the Examiner meets the burden of establishing the lack of utility by making evidence of record that conclusively refutes the Applicants asserted utility.

The Action also argues that "The specification fails to disclose any specific biological or

chemical function for the polypeptide of SEQ ID NO:4, .." This is incorrect as the protein of the instant invention belongs to a family of compounds with a common, well established specific and substantial utility. The present application describes a metalloprotease. The utility of metalloproteases are well known to the art (see, for example, U.S. Patent Nos. 6,399,371; 6,391,610), as are inhibitors (see, for example, U.S. Patent Nos. 6,339,092; 6,417,219; 6,420,415), assays and methods of use.

The legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable. According to the Examination Guidelines for the Utility Requirement, if the applicant has asserted that the claimed invention is useful for any particular purpose (i.e., it has a "specific and substantial utility") and the assertion would be considered credible by a person of ordinary skill in the art, the Examiner should not impose a rejection based on lack of utility (66 Federal Register 1098, January 5, 2001).

Applicants have described sequences that encode a novel human protease, a metalloprotease known as ADAM-TS15, the tissue specific expression pattern (page 3, line 37-33) and naturally occurring polymorphisms (page 17, lines 12-18) that exist within the sequences of the present invention.

As evidence of the credibility of Applicants assertion that the present invention is a metalloprotease, in particular a variant of ADAM-TS15, Applicants submit evidence that a sequence that is 100% identical at the amino acid level to SEQ ID NO:4 of the present invention over its entire 950 amino acid sequence is present in GenBank, the world's largest repository of such information. This protein, GenBank accession number NP_620686.1, has been annotated by third party scientists, wholly unaffiliated with Applicants, as encoding a disintegrin-like and metalloprotease (reprolysin type) with thrombospondin type 1 motif, 15 preproprotein [*Homo sapiens*] (description and amino acid alignment and GeneBank report provided as **Exhibit A**).

Given this clear and convincing evidence that those of skill in the art would recognize the present invention as a metalloprotease, more specifically ADAM-TS15, which is described in the scientific publication entitled "Cloning, expression analysis, and structural characterization of seven novel human ADAMTSs, a family of metalloproteinases with disintegrin and thrombospondin-1 domains." (Cal *et al.*, Gene **283**, 49-62, 2002, abstract provided as **Exhibit B**). Clearly, there can be no question that Applicants' asserted utility for the described sequences is "credible." Applicants have thus supplied evidence supporting their assertion that those of skill in the art would recognize that the

sequences of the present invention encode a metalloprotease, more particularly that of ADAMTS15, and that it therefore has all the recognized uses thereof. In contrast, the Examiner has provided no evidence of record indicating that those of skill in the art would not recognize that the sequences of the present invention encode a metalloprotease. As such, the scientific evidence clearly establishes that Applicants have described an invention whose utility is in full compliance with the provisions of 35 U.S.C. § 101, and the Examiner's rejection should be withdrawn.

Furthermore, the real world utility of the present invention is further demonstrated by results obtained when a knockout mouse was made using techniques described in the specification (page 2, line 34 and page 18, lines 30-32) in which the mouse gene encoding the ortholog of human a disintegrin-like and metalloprotease (reprolysin type) with thrombospondin type 1 motif, 15 (ADAMTS15) was disrupted in embryonic stem cells. Knockout mice prepared as described in the specification as filed and gene disruption was confirmed by Southern blot. The mice were subject to a medical work-up using an integrated suite of medical diagnostic procedures designed to assess the function of the major organ systems in a mammalian subject. Disruption of the mouse gene encoding the present invention and thus elimination of the protein it encodes, metalloprotease ADAMTS15, resulted in immunological abnormalities in homozygous (-/-) knockout mice. More specifically, the homozygous (-/-) mice exhibited an increased mean serum IgG2a response to ovalbumin challenge when compared with their wild-type (+/+) littermates, in which the gene was still functional. Homozygous (-/-) knockout mice also exhibited increased mean serum IL-6 and TNF-alpha responses to LPS challenge when compared with their wild-type (+/+) littermates and historical means. This clearly provides evidence that the nucleic acid and protein of the present invention have a biological function and the molecules of the present invention as well as agonists or antagonists directed at them can be used to diagnose and treat arthritis, asthma, connective tissue and other immune mediated disorders (as stated in the specification at least at page 13, line 27-29), validated drug targets. Thus clearly the molecules of the present invention also have real world substantial and specific utility as having been identified as biologically validated drug targets (specification page 8, line 8)using methods and identified for diseases and disorders asserted in the specification as filed. Thus clearly the molecules of the present invention also has real world substantial and specific utility.

Furthermore, clearly if no other information had been provided, the use of the polymorphisms

described in the application (at page 17, lines 12-18) would have provided specific and substantial utility to the present sequences. Several polymorphisms were identified including a G/C polymorphism at the nucleotide position represented by, for example, position 491 of SEQ ID NO: 3 (which can result in a gly or ala at the region corresponding to amino acid (aa) position 164 of, for example, SEQ ID NO:4), and a T/G at nucleotide position 2598 (which can result in a cys or trp at aa position 513). Clearly this indicates that the present nucleic acid sequences had utility in forensic analysis, as described in the specification as originally filed. As such polymorphisms are the basis for forensic and paternity analysis, which are undoubtedly "real world" utilities, the presently claimed sequence logically must in itself be useful.

Applicants respectfully point out that the presently described polymorphisms can be used by those skilled in the art to "distinguish between one person from another" simply based on the presence or absence of the described polymorphisms. Thus the skilled artisan would be able to use the presently described polymorphisms in forensic analysis exactly as they were described in the specification as originally filed (for example on page 3, line 10), without **any** additional research. It is important to note that simply because the use of these polymorphic markers will necessarily provide additional information on the percentage of particular subpopulations that contain these polymorphic markers does not mean that additional research is needed in order for these markers as they are presently described in the instant specification to be used in forensic analysis (which is not, as the Action suggests (at page 4, line 14) a research use.

Even in the worst case scenario, the described polymorphisms are each useful to distinguish 50% of the population (in other words, the marker being present in half of the population). The ability of a polymorphic marker to distinguish at least 50% of the population is an inherent feature of any polymorphic marker, and this feature is well understood by those of skill in the art. Applicants note that as a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands*, 8 USPQ 2d 1400 (Fed. Cir. 1988).

Applicants respectfully point out that all that is required to support Applicants' assertion of utility is for the skilled artisan to believe that the presently described polymorphic markers could be useful in forensic analysis. The fact that forensic biologists use polymorphic markers such as those described by Applicants every day provides more that ample support for the assertion that forensic

biologists would also be able to use the specific polymorphic markers described by Applicants in the same fashion. Therefore, these allegations are completely without merit, and in no way establish that the present invention lacks utility.

The fact that other polymorphic markers have been identified in other genetic loci, or that the use of the presently described polymorphic markers will provide additional information concerning the prevalence of these markers in certain subpopulations, does not mean that Applicants' identification of polymorphic markers in SEQ ID NO:1 is not specific. As clearly stated by the Federal Circuit in *Carl Zeiss Stiftung v. Renishaw PLC*, 20 USPQ2d 1101 (Fed. Cir. 1991):

> An invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications: "[T]he fact that an invention has only limited utility and is only operable in certain applications is not grounds for finding a lack of utility." *Envirotech Corp. v. Al George, Inc.*, 221 USPQ 473, 480 (Fed. Cir. 1984)

In other words, just because other (possibly better) polymorphic markers from the human genome have been described, or that additional information about the presently described polymorphic markers can be gained through the use of these markers, does not establish that the presently described polymorphic markers lack a specific utility. The requirement for a **specific** utility, which is part of the standard for utility under 35 U.S.C. § 101 presently being applied by the Office, should not be confused with the requirement for a **unique** utility, which is not the legal standard. If every invention were required to have a unique utility, the Patent and Trademark Office would no longer be issuing patents on batteries, automobile tires, golf balls, golf clubs, and treatments for a variety of human diseases, just to name a few particular examples, because other examples of each of these have already been described and patented. However, only the briefest perusal of virtually any issue of the Official Gazette provides numerous examples of patents being granted on each of the above compositions every week. Furthermore, if each invention needed to have a unique utility in order to be patented, the entire class and subclass system would be an effort in futility, as the class and subclass system serves solely to group such common inventions, which would not be required if each invention needed to have a unique utility. In view of the above standards and "common sense" analysis, there can be little question that the present sequence clearly meets the requirements of 35 U.S.C. § 101.

Furthermore, as the presently described polymorphism is a part of the family of polymorphisms that have a well established utility, the Federal Circuit's holding in *In re Brana,* (34 USPQ2d 1436 (Fed. Cir. 1995), "*Brana*") is directly on point. In *Brana*, the Federal Circuit admonished the Patent and Trademark Office for confusing "the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption". *Brana* at 1442. The Federal Circuit went on to state:

> At issue in this case is an important question of the legal constraints on patent office examination practice and policy. The question is, with regard to pharmaceutical inventions, what must the applicant provide regarding the practical utility or usefulness of the invention for which patent protection is sought. This is not a new issue; it is one which we would have thought had been settled by case law years ago.

Brana at 1439, emphasis added. The choice of the phrase "utility or usefulness" in the foregoing quotation is highly pertinent. The Federal Circuit is evidently using "utility" to refer to rejections under 35 U.S.C. § 101, and is using "usefulness" to refer to rejections under 35 U.S.C. § 112, first paragraph. This is made evident in the continuing text in *Brana*, which explains the correlation between 35 U.S.C. §§ 101 and 112, first paragraph. The Federal Circuit concluded:

> FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws. Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer.

Brana at 1442-1443, citations omitted, emphasis added. As set forth above, the present polymorphisms are useful in forensic analysis as described in the specification as originally filed, without the need for any further research. As discussed above, even if the use of these polymorphic markers

provided additional information on the percentage of particular subpopulations that contain these polymorphic markers, this would not mean that "additional research" is needed in order for these markers as they are presently described in the instant specification to be of use to forensic science. As stated above, using the polymorphic marker as described in the specification as originally field can definitely distinguish members of a population from one another. However, even if, *arguendo*, further research might be required in certain aspects of the present invention, this does not preclude a finding that the invention has utility, as set forth by the Federal Circuit's holding in *Brana*, which clearly states, as highlighted in the quote above, that "pharmaceutical inventions, necessarily includes the expectation of further research and development" (*Brana* at 1442-1443, emphasis added). In assessing the question of whether undue experimentation would be required in order to practice the claimed invention, the key term is "undue", not "experimentation". *In re Angstadt and Griffin*, 190 USPQ 214 (CCPA 1976). The need for some experimentation does not render the claimed invention unpatentable. Indeed, a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin*, *supra*; *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). Again, as a matter of law, it is well settled that a patent need not disclose what is well known in the art (*In re Wands*, *supra*).

Although Applicants need only make one credible assertion of utility to meet the requirements of 35 U.S.C. § 101 (*Raytheon v. Roper*, 220 USPQ 592 (Fed. Cir. 1983); *In re Gottlieb*, 140 USPQ 665 (CCPA 1964); *In re Malachowski*, 189 USPQ 432 (CCPA 1976); *Hoffman v. Klaus*, 9 USPQ2d 1657 (Bd. Pat. App. & Inter. 1988)), as a further example of the utility of the sequences of the present invention in chromosome mapping (specification at least at page 3, line 4), in localizing the specific region of the human chromosome which encodes the present invention as well as identification of functionally active intron/exon splice junctions (specification at least at page 11, lines 24-29)is the evidence provided in **Exhibit** C. The present nucleotide sequence has a specific utility that was demonstrated in the specification as filed in identification of protein coding sequence and chromosome mapping. When SEQ ID NO:3 was overlain on known human genomic sequence it can be used to map the 8 non-contiguous protein encoding exons of the gene comprising the presently claimed sequence to chromosome 11 (partially present within a chromosome 11 BAC clone; GenBank Accession Number AP002986.2 entitled *Homo sapiens* genomic DNA, chromosome 11q, clone:

RP11-121M22, complete sequence and AP003459.2, entitled *Homo sapiens* genomic DNA, chromosome 11q, clone: RP11-211H5, complete sequence (alignment presented in **Exhibit C**). As the 8 different protein coding regions are non-contiguously encoded along the chromosome clearly one would not simply be able to identify the 8 protein encoding exons that make up the sequence of the present intention from within the large genomic sequence. Nor, would one be able to map the protein encoding regions identified specifically by the sequences of the present invention without knowing exactly what those specific sequences were.

As only a minor percentage (2-4%) of the genome actually encodes exons, which in-turn encode amino acid sequences. The presently claimed polynucleotide sequence provides biologically validated empirical data (*e.g.*, showing which sequences are transcribed, spliced, and polyadenylated) that *specifically* define that portion of the corresponding genomic locus that actually encodes exon sequence. Equally significant is that the claimed polynucleotide sequence defines how the encoded exons are actually spliced together to produce an active transcript (*i.e.*, the described sequences are useful for functionally defining exon splice-junctions). Such biologically validated splice junctions are superior to splice junctions that may have been predicted from genomic sequence alone, and, as detailed in the specification, at least at page 11, lines 24-29, that "sequences derived from regions adjacent to the intron/exon boundaries of the human gene can be used to design primers for use in amplification assays to detect mutations within the exons, introns, splice sites (*e.g.*, splice acceptor and/or donor sites), *etc.*, that can be used in diagnostics and pharmacogenomics". Applicants respectfully submit that the practical scientific value of biologically validated, expressed, spliced, and polyadenylated mRNA sequences, that encodes a novel human metalloprotease, ADAMTS15, that is expressed in some tissues but not others, is readily apparent to those skilled in the relevant biological and biochemical arts.

Clearly, the present polynucleotide provides exquisite specificity in localizing the specific region of human chromosome 11 that contains the gene encoding the given polynucleotide, a utility not shared by virtually any other nucleic acid sequences. In fact, it is this specificity that makes this particular sequence so useful. Early gene mapping techniques relied on methods such as Giemsa staining to identify regions of chromosomes. However, such techniques produced genetic maps with a resolution of only 5 to 10 megabases, far too low to be of much help in identifying specific genes involved in

disease. The skilled artisan readily appreciates the significant benefit afforded by markers that map a specific locus of the human genome, such as the present nucleic acid sequence. For further evidence in support of the Applicants' position, see for example, section 3 of Venter *et al.* (2001, Science *291*:1304, at pp. 1317-1321, including Fig. 11 at pp.1324-1325), which demonstrates the significance of expressed sequence information in the structural analysis of genomic data. The presently claimed polynucleotide sequence defines a biologically validated sequence that provides a unique and specific resource for mapping the genome essentially as described in the Venter *et al.* article. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

An additional utility includes the use of the presently claimed polynucleotides on DNA chips. Further, the Action seems to be requiring Applicants to identify the biological role of the nucleic acid or function of the protein encoded by the presently claimed polynucleotides before the present sequences can be used in gene chip applications that meet the requirements of § 101. Applicants respectfully point out that knowledge of the exact function or role of the presently claimed sequence is not required to track expression patterns using a DNA chip. Given the widespread utility of such "gene chip" methods using *public domain* gene sequence information, there can be little doubt that the use of the presently described *novel* sequences would have great utility in such DNA chip applications. The claimed sequence provides a specific marker of the human genome (see evidence below), and that such specific markers are targets for discovering drugs that are associated with human disease. The described polymorphism furthermore enhances the utility of the sequences of the present invention. This polymorphism has particular, specific utility in DNA gene chip based analysis as they have been identified to contain several coding region single nucleotide polymorphisms (cSNPs), thus increasing their utility in DNA gene chip based analysis.

Evidence of the "real world" substantial utility of the present invention is further provided by the fact that there is an entire industry established based on the use of gene sequences or fragments thereof in a gene chip format. Perhaps the most notable gene chip company is Affymetrix. However, there are many companies which have, at one time or another, concentrated on the use of gene sequences or fragments, in gene chip and non-gene chip formats, for example: Gene Logic, ABI-Perkin-Elmer, HySeq and Incyte. In addition, one such company, Rosetta Inpharmatics, was viewed to have such "real world" value that it was acquired by large pharmaceutical company, Merck & Co., for substantial

sums of money (net equity value of the transaction was $620 million). The "real world" substantial industrial utility of gene sequences or fragments would, therefore, appear to be widespread and well established. Clearly, persons of skill in the art, as well as venture capitalists and investors, readily recognize the utility, both scientific and commercial, of genomic data in general, and specifically human genomic data. Billions of dollars have been invested in the human genome project, resulting in useful genomic data (see, *e.g.*, Venter *et al.*, 2001, Science *291*:1304). The results have been a stunning success as the utility of human genomic data has been widely recognized as a great gift to humanity (see, *e.g.*, Jasny and Kennedy, 2001, Science *291*:1153). Clearly, the usefulness of human genomic data, such as the presently claimed nucleic acid molecules, is substantial and credible (worthy of billions of dollars and the creation of numerous companies focused on such information) and well-established (the utility of human genomic information has been clearly understood for many years). The sequences of the present invention have particularly specific utility in DNA gene chip based analysis because they encode a novel human metalloprotease, ADAMTS15, a protein of well-recognized function, their tissue specific expression pattern has been described and because they have been identified to contain coding region nucleotide polymorphisms (see above), thus increasing their utility in DNA gene chip based analysis.

Thus, those skilled in the art would instantly recognize that the present nucleotide sequence would be an ideal, novel candidate for assessing gene expression using, for example, DNA chips, as the specification details. Such "DNA chips" clearly have utility, as evidenced by hundreds of issued U.S. Patents, as exemplified by U.S. Patent Nos. 5,445,934, 5,556,752, 5,744,305, as well as more recently issued U.S. Patent Nos. 5,837,832, 6,156,501 and 6,261,776. Accordingly, the present sequence has a specific utility in such DNA chip applications. Clearly, compositions that enhance the utility of such DNA chips, such as the presently claimed nucleotide sequence, must also be useful.

Finally, while Applicants are well aware of the new Utility Guidelines set forth by the USPTO, Applicants respectfully point out that the current rules and regulations regarding the examination of patent applications is and always has been the patent laws as set forth in 35 U.S.C. and the patent rules as set forth in 37 C.F.R., not the Manual of Patent Examination Procedure or particular guidelines for patent examination set forth by the USPTO. Furthermore, it is the job of the judiciary, not the USPTO, to interpret these laws and rules. Applicants are unaware of any significant recent changes in either 35

U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit that is in keeping with the new Utility Guidelines set forth by the USPTO. This is underscored by numerous patents that have been issued over the years that claim nucleic acid fragments that do not comply with the new Utility Guidelines. Examples of such issued U.S. Patents, include U.S. Patent Nos. 5,817,479, 5,654,173, and 5,552,281 (each of which claims short polynucleotides), and recently issued U.S. Patent No. 6,340,583 (which includes no working examples), none of which contain examples of the specific, substantial or "real-world" utilities that the Examiner seems to be requiring in the present case. As issued U.S. Patents are presumed to meet all of the requirements for patentability, including 35 U.S.C. §§ 101 and 112, first paragraph (see below), Applicants submit that the present polynucleotides must also meet the requirements of 35 U.S.C. § 101. While Applicants agree that each application is examined on its own merits, Applicants are unaware of any changes to 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit, since the issuance of these patents that render the subject matter claimed in these patents, which is similar to the subject matter in question in the present application, as suddenly non-statutory or failing to meet the requirements of 35 U.S.C. § 101. Given the rapid pace of development in the biotechnology arts, it is difficult for the Applicants to understand how an invention fully disclosed and free of prior art at the time the present application was filed, could somehow retain *less* utility and be *less* enabled than inventions in the cited issued U.S. patents (which were filed during a time when the level of skill in the art was clearly lower). Simply put, Applicants invention is *more* enabled and retains *at least as much* utility as the inventions described in the claims of the U.S. patents of record. Thus, holding Applicants to a different standard of utility would be arbitrary and capricious, and, like other clear violations of due process, cannot stand.

Therefore, for each of the above reasons the sequences of the present invention have been shown to have specific, substantial real world utility and thus the present rejection of the pending claims under 35 U.S.C. § 101 has been avoided. Applicants, therefore, respectfully request withdrawal of the pending rejection.

V. Rejection of Claims Under 35 U.S.C. § 112, First Paragraph

The Action also rejects claims 1-4 and 6 under 35 U.S.C. § 112, first paragraph, allegedly

since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention.

Applicants respectfully submit that the claimed invention has been shown to have "a specific, substantial, and credible utility", as detailed in the section above. Therefore, one skilled in the art would clearly know how to use the claimed invention and Applicants therefore request that the rejection of claims. Therefore, Applicants submit that as the presently claimed sequence molecules have been shown to have a substantial, specific, credible and well-established utility, and thus the rejection of the pending claims under 35 U.S.C. § 112, first paragraph has been avoided. Thus, Applicants respectfully request that the rejection be withdrawn.

VI. Rejection of Claims 1-3 Under 35 U.S.C. § 112, First Paragraph

The Action next rejects claim 1-3 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This rejection is allegedly based on the finding that claims 1-3 are directed at nucleic acids comprising at least 24 contiguous bases. However, only original claim 1 contains any such reference. Applicant's comments will therefore be directed at this issue but note that it is only applicable to original Claim 1.

35 U.S.C. § 112, first paragraph, requires that the specification contain a written description of the invention. The Federal Circuit in *Vas-Cath Inc. v. Mahurkar* (19 USPQ2d 1111 (Fed. Cir. 1991); "*Vas-Cath*") held that an "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*." *Vas-Cath*, at 1117, emphasis in original. However, it is important to note that the above finding uses the terms reasonable clarity to those skilled in the art. Further, the Federal Circuit in *In re Gosteli* (10 USPQ2d 1614 (Fed. Cir. 1989); "*Gosteli*") held:

> Although [the applicant] does not have to describe exactly the subject matter claimed, . . . the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.

Gosteli at 1618, emphasis added. Additionally, *Utter v. Hiraga* (6 USPQ2d 1709 (Fed. Cir. 1988);

"*Utter*"), held "(a) specification may, within the meaning of 35 U.S.C. § 112 ¶1, contain a written description of a broadly claimed invention without describing all species that claim encompasses" (*Utter*, at 1714). Therefore, all Applicants must do to comply with 35 U.S.C. § 112, first paragraph, is to convey the invention with reasonable clarity to the skilled artisan.

Further, the Federal Circuit has held that an adequate description of a chemical genus "requires a precise definition, such as by structure, formula, chemical name or physical properties" sufficient to distinguish the genus from other materials. *Fiers v. Sugano*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993; "*Fiers*"). *Fiers* goes on to hold that the "application satisfies the written description requirement since it sets forth the . . . nucleotide sequence" (*Fiers* at 1607). In other words, provision of a structure and formula - the nucleotide sequence - renders the application in compliance with 35 U.S.C. § 112, first paragraph.

More recently, the standard for complying with the written description requirement in claims involving chemical materials has been explicitly set forth by the Federal Circuit:

> In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. *Univ. of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Thus, a claim describing a genus of nucleic acids by structure, formula, chemical name or physical properties sufficient to allow one of ordinary skill in the art to distinguish the genus from other materials meets the written description requirement of 35 U.S.C. § 112, first paragraph. As further elaborated by the Federal Circuit in *Univ. of California v. Eli Lilly and Co.*:

> In claims to genetic material ... a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA', without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art cannot, as one can do with a fully described genus, visualize or recognize the identity of members of the genus. (Emphasis added)

Thus, as opposed to the situation set forth in *Univ. of California v. Eli Lilly and Co.* and *Fiers*, the

nucleic acid sequences of the present invention are not distinguished on the basis of function, or a method of isolation, but in fact are distinguished by structural features - a chemical formula, *i.e.*, the *sequence itself.*

Using the nucleic acid sequences, or amino acid sequences, of the present invention (as set forth in the Sequence Listing), the skilled artisan would readily be able to distinguish the claimed nucleic acids, or amino acids, from other materials on the basis of the specific structural description provided. Polynucleotides comprising 24 consecutive nucleic acids of the nucleotide sequence of, for example, SEQ ID NO:3 or a nucleotide sequence that encodes the amino acid sequence of SEQ ID NO:4, are within the genus of the instant claims, while those that lack this structural feature lie outside the genus. Thus those of skill in the art would have known how to make and use the invention as claimed in original Claim 1, however, as this claim has been amended to read on the full-length molecule this rejection has been rendered moot and respectfully request withdrawal of the rejection.

VII. Rejection of Claims 1-3 Under 35 U.S.C. § 112, First Paragraph

The Action rejects claims 1-3 under 35 U.S.C. § 112, first paragraph, as allegedly the disclosure is not enabling for any embodiment. This rejection is allegedly based on the finding that claims 1-3 are directed at nucleic acids comprising at least 24 contiguous bases. However, only original claim 1 contains any such reference and this was addressed in the previous section and amendment of Claim 1 has rendered this rejection rendered moot. Applicants, therefore, respectfully request withdrawal of this rejection.

VIII. Rejection of Claim 2 Under 35 U.S.C. § 112, Second Paragraph

The Action rejects claim 2 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 2 stands rejected because the phrase "stringent conditions" is alleged to be indefinite. Although Applicants believe that this claim as originally filed sufficiently points out and distinctly claims the invention, in order to more rapidly progress the case to allowance, Applicants have amended Claim 2 to specify "highly" stringent conditions. Highly stringent conditions for full length molecules are defined in the specification on page 5, lines 1-8. Applicants, therefore, respectfully submit that this

rejection has been avoided by Applicant's amendment of Claim 2 to specify "highly" stringent conditions. Accordingly, the Examiner is respectfully requested to withdraw the pending rejection of Claim 2 under 35 U.S.C. § 112, second paragraph.

IX. Rejection of Claim 1 Under 35 U.S.C. § 102(e)

The Action rejects Claim 1 under 35 U.S.C. § 102(b), as being anticipated by Mahairas, *et al.* (accession number AQ809642). While Applicants do not necessarily agree with the present rejection, as Claim 1 has been amended to recite the complete nucleotide sequence of SEQ ID NO:3, which is not taught by Mahairas, Applicants submit that the rejection of Claim 1 under 35 U.S.C. § 102(b) has been thus avoided, and respectfully request withdrawal of the rejection.

The Action next rejects Claims 1-3 under 35 U.S.C. § 102(e), as being anticipated by WO 01/98468 (Yue, *et al.*). While Applicants do not necessarily agree with the present rejection, as Claim 1 has been amended to recite the complete nucleotide sequence of SEQ ID NO:3, which is not taught by WO 01/98468 (Yue, *et al.*), Applicants submit that the rejection of Claim 1 under 35 U.S.C. § 102(e) has been thus avoided, and respectfully request withdrawal of the rejection.

X. Conclusion

The present document is a full and complete response to the Action. In conclusion, Applicants submit that, in light of the foregoing remarks, the present case is in condition for allowance, and such favorable action is respectfully requested. Should Examiner Nashed have any questions or comments, or believe that certain amendments of the claims might serve to improve their clarity, a telephone call to the undersigned Applicants' representative is earnestly solicited.

Respectfully submitted,

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Date

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